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3-Methoxy-19-norpentara-1,3,5(10),17(20)-tetraen-21-one

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Key indicators

Single-crystal X-ray study
T = 123 K
Mean σ(C–C) = 0.004 Å
R factor = 0.034
wR factor = 0.073
Data-to-parameter ratio = 9.0

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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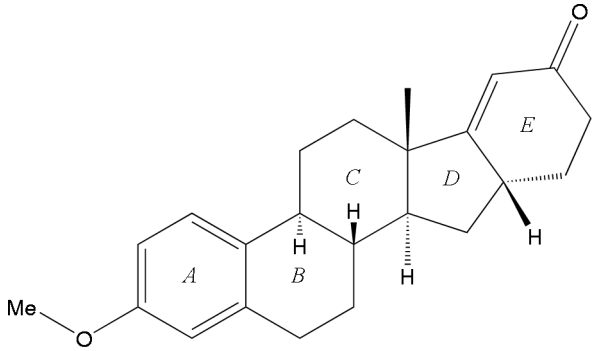
In the title compound, alternatively called 3′-oxocyclohex-1′-eno-1′,6′:16,17–3-*O*-methylestra-1,3,5(10),16(16*H*)-tetraen-3-ol, $C_{23}H_{28}O_2$, the cyclohexenone ring is fused to the five-membered ring through the α position at C16. As a result of the ring annelation, the distance between carbonyl and methoxy O atoms [12.994 (2) Å] is much longer than that in estrones or estradiol. The crystal packing is stabilized by C—H···O and C—H···π hydrogen-bonding interactions.

Comment

The title compound, (I), was synthesized by Allison *et al.* (1967) as a potential anti-inflammatory agent. At the time, the stereochemistry of the introduced chirality at C16 was determined through ORD spectroscopic analysis of the *n*–π* transition of the C17(20)-en-21-one system. An X-ray crystal structure analysis of (I) was carried out in order to better understand interactions of (I) with steroidal receptors.



(I)

Ring *A* (Fig. 1) is essentially planar, as observed in other estrones and estradiols. Ring *B* has a half-chair conformation, with Cremer & Pople (1975) puckering parameters *Q* = 0.507 (3) Å, θ = 47.5 (3)° and φ = 154.1 (4)°. This conformation

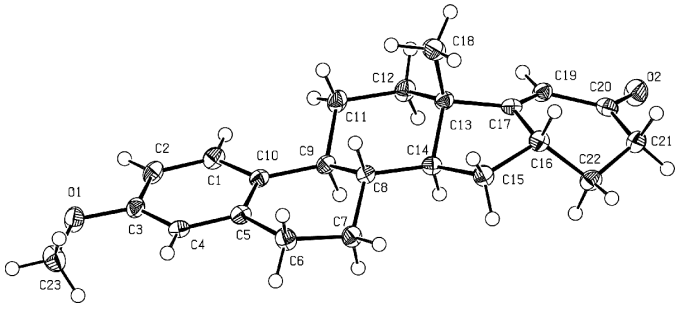


Figure 1
View of (I) (Spek, 2003), showing 50% probability displacement ellipsoids and the atomic numbering.

is also in accordance with the relative signs of the endocyclic torsion angles within ring *B* (Boeyens, 1978). Ring *C* adopts the chair conformation [Q = 0.588 (3) Å, θ = 4.2 (3)° and φ = 311 (3)°]. Ring *D* is in a half-chair conformation [Q = 0.451 (3) Å and φ = 191.0 (3)°], with a pseudorotation angle Δ = 352.0 (2)°, and a maximum torsion angle φ = 46.4 (1)° (Rao *et al.*, 1981) for the atom sequence C13—C14—C15—C16—C17.

Ring *E* adopts an envelope conformation with puckering parameters Q = 0.474 (3) Å, θ = 55.7 (3)° and φ = 301.8 (4)°. Ring *E* is connected to ring *D* through the α position at C16. This stereochemistry at C16 had been determined by Allison *et al.* (1967) correctly through the ORD measurements (see above). Atoms C17, C19, C20 and O2 are coplanar [C17—C19—C20—O2 = −178.2 (2)°] due to the π conjugation of the enone moiety. Atom C22 is out of plane, minimizing the ring strain to give the envelope conformation of ring *E*.

Typically, the oxygen at C3 (O1) and the oxygen on the ring furthest from ring *A* (oxygen at C17 in estrone and estradiols) significantly influence the binding of the steroid to the steroidal receptor. In common estra-1,3,5(10)-trien-17-one (estrone) derivatives, the direction of the C=O bond is almost parallel to the plane determined by ring *A* or slightly directed towards the α-side of that plane [C3—C2—C17—O2 torsion angles range from −168.3 to −178.9°, with an average of −174° (van den Bossche, 1971; Busetta *et al.*, 1973; Debaerdemaeker, 1972)]. In (I), the corresponding torsion angle C3—C2—C20—O2 is −159.4 (2)°, which is much larger than in usual estrones (see above), but less than in other estra-3,17α-diol derivatives (124.2 and 117.3° for C3—C2—C17—O2; Busetta *et al.*, 1976).

As a result of the *E*-ring annelation, the O1···O2 distance of 12.994 (2) Å in (I) is much longer than that in estrones [10.79–10.90 Å, average 10.83 Å; van den Bossche, 1971; Busetta *et al.*, 1973; Debaerdemaeker, 1972], estra-3,17α-diols (10.54 and 10.32 Å; Busetta *et al.*, 1976) and estra-3,17β-diols (10.83–11.06 Å, average 10.99 Å; Bolaños-García *et al.*, 1996; Busetta, Courseille *et al.*, 1972; Busetta & Hospital, 1972; Duax, 1972; Parrish & Pinkerton, 1999; Parrish, 2003; Prokai *et al.*, 2001; Punzi *et al.*, 1992; Reck *et al.*, 1986; Starova *et al.*, 2001; Tsukuda *et al.*, 1968; Vichard *et al.*, 1992; Zacharias *et al.*, 1995).

In the crystal structure, molecules translated by a unit along the *c* axis are linked by C4—H4···O2^{i} hydrogen bonds to form a chain. Adjacent chains are linked *via* C9—H9···O2^{ii} hydrogen bonds and C22—H22*A*···*Cg*1^{iii} (*Cg*1 is the C1–C6 ring centroid) interactions to form a layered structure. Symmetry codes and the geometry for these interactions are given in Table 1.

Experimental

Compound (I) was prepared by the Robinson annelation procedure from 16-hydroxymethylidene-3-methoxyestra-1,3,5(10)-trien-17-one by a known procedure (Allison *et al.*, 1967). The crystal used for X-ray structure analysis was obtained by recrystallization of (I) from chloroform–ether–hexane (1:1:1).

Crystal data

$C_{23}H_{28}O_2$
M_r = 336.47
Orthorhombic, $P2_12_12_1$
a = 10.980 (4) Å
b = 12.499 (4) Å
c = 12.865 (4) Å
V = 1765.5 (10) Å^3
Z = 4
D_x = 1.266 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 5425 reflections
θ = 3.2–27.5°
μ = 0.08 mm^{-1}
T = 123.1 K
Prism, colourless
0.16 × 0.12 × 0.05 mm

Data collection

Rigaku Saturn diffractometer
ω scans
Absorption correction: multi-scan (Jacobson, 1998)
T_{min} = 0.879, T_{max} = 0.996
14467 measured reflections
2295 independent reflections
1431 reflections with $F^2 > 2\sigma(F^2)$
R_{int} = 0.053
θ_{max} = 27.5°
$h = -14 \rightarrow 14$
$k = -16 \rightarrow 16$
$l = -13 \rightarrow 16$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.034
$wR(F^2)$ = 0.073
S = 1.00
2295 reflections
255 parameters
All H-atom parameters constrained
$w = 1/[0.3590\sigma(F_o^2)]/(4F_o^2)$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.26 e Å^{-3}
$\Delta\rho_{min}$ = −0.21 e Å^{-3}
Extinction correction: Larson (1970), equation 22
Extinction coefficient: 54.9 (11)

Table 1
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
C4—H4···O2^{i}	0.93	2.54	3.410 (3)	155
C9—H9···O2^{ii}	0.98	2.69	3.627 (3)	160
C22—H22*A*···*Cg*1^{iii}	0.97	2.52	3.414 (3)	152

Symmetry codes: (i) $x, y, z-1$; (ii) $\frac{1}{2}-x, -y, z-\frac{1}{2}$; (iii) $\frac{1}{2}-x, -y, \frac{1}{2}+z$. *Cg*1 is the C1–C6 ring centroid.

H atoms were placed in calculated positions (C—H = 0.93–0.98 Å) and were included in the refinement in the riding-model approximation, with U_{iso}(H) values set at 1.2U_{eq}(carrier atom). In the absence of significant anomalous dispersion effects, Friedel pairs were averaged. The absolute configuration was assigned from that of the starting material in the synthesis.

Data collection: *CrystalClear* (Rigaku, 1999); cell refinement: *CrystalClear*; data reduction: *CrystalStructure* (Rigaku/MSC, 2004); program(s) used to solve structure: *SIR*97 (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *CrystalStructure*.

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